REMARKS

Claims 1-5 are pending. Claims 4 and 5 have been withdrawn from consideration.

In the Office Action mailed April 2, 2008, claims 1-3 have been rejected as allegedly obvious under 35 U.S.C. § 103 over U.S. Patent No. 6,379,669 to Sinha et al. ("*Sinha*") in view of *Davenas*, *Epshtein*, and *Feldman* (of record).

By this Amendment, Applicants amended claims 1 and 2, cancelled claim 3, and added new claims 6-9. Applicants respectfully request reconsideration and allowance of all pending claims in view of the amendments and remarks set forth below.

I. AMENDED CLAIM 1 IS SUPPORTED IN THE APPLICATION AS FILED

As amended, claim 1 now recites:

> 1. (Currently Amended) A medicament for ~~effective in~~ treating a ~~prostate~~ disease of prostate, said medicament comprising a homeopathically activated ~~one or more homeopathic dilutions of potentiated~~ form of at least one monoclonal, polyclonal, or natural antibody~~ies~~ to a prostate specific antigen (PSA)~~,~~ ~~wherein one or more of the homeopathic dilutions of the potentiated~~ form ~~of antibodies to the prostate specific antigen being obtained by a homeopathic potentiation technology~~.

Applicants are fully aware that the newly added limitation "homeopathically activated" is not set forth in the application in *ipsis verbis*. For this reason and to advance the prosecution on the merits, Applicants wish to address the issue preemptively and directly for Examiner's consideration.

Applicants note that *haec verbis* disclosure is not a pre-requisite for complying with the written description requirement. *See* MPEP § 2163. I. B. The description may be express, implicit, or inherent. *Id.* The key to evaluating compliance with the written description requirement is a determination whether the applicant had possession of the claimed invention based on the content of the application as a whole. *See* MPEP § 2163.

II. The outcome of the evaluation depends on whether "the description clearly allows persons of ordinary skill in the art to recognize that he or she invented what is claimed." *See* MPEP § 2163.01, *citing In re Gostelli*, 872 F.2d 1008, 1012 (Fed. Cir. 1989).

The specification describes: a) preparation of "activated" or "potentiated" antibodies to PSA antigen by homeopathic technology (*e.g.*, Example 1), b) administration of the activated or potentiated form of the PSA antibody to patients (*e.g.*, Examples 3 and 4), and c) biological effects of such administration on prostate tissues (*e.g.*, Examples 1 and 2). In combination, these disclosures clearly place "homeopathically activated form" of the antibodies in possession of the inventors as of the filing date of the above-identified application.

Therefore, Applicants respectfully submit that amended claim 1 is fully supported in the application as filed.

II. OBVIOUSNESS REJECTION OVER *SINHA* IN VIEW OF *DAVENAS, EPSHTEIN,* AND *FELDMAN*

The Examiner has rejected claims 1-3 as allegedly obvious.

Sinha teaches PSA antibodies at normal concentrations. *Davenas* teaches that human basophile degranulation is triggered by dilute IgE antiserum. *Feldman* teaches treatment of rheumatoid arthritis with anti-TNF antibodies.

Epshtein discloses an effect of ultra-low doses of antibodies to brain-specific antigen (S-100) on behavior characteristics in rat. *Epshtein* reports that administration of the antibody led to changes in rat behavior for a partial group of rats in the study (for example, an increase in the latent period of the emotional reflex reaction).

In the Office Action, the Examiner appears to suggest that one skilled in the art would be motivated to combine *Sinha* with *Davenas* and/or *Epshtein* based on the motivation of *Feldman*, *i.e.*, the use the PSA antibodies of *Sinha* in the manner disclosed in *Epshtein* and/or *Davenas*. The Examiner also suggests that one skilled in the art would have a reasonable expectation that such combination/modification would be successful.

Applicants strongly and respectfully disagree.

To set forth a *prima facie* case of obviousness, the Examiner must show that one skilled in the art would have a reasonable expectation that the combination of *Sinha* and *Epshtein/Davenas* will be successful. *See* § MPEP 2143.02. Meeting the burden requires that the prior art provides some degree of predictability. *Id.*, *citing In re Rhinehart*, 531 F.2d 1048, 189 USPQ 143 (CCPA 1976). In the pharmaceutical arts, the expectation of success is reasonable when the prior art as a whole would lead one skilled in the art to believe that the claimed invention would at least have activity of some type for the stated purpose. *In re O'Farrell*, 853 F.2d 984, 903 (Fed. Cir. 1988), *In re Merck*, 800 F.2d 1091, 1097 (Fed. Cir. 1986). The Court of Appeals for the Federal Circuit suggested that finding of reasonable expectation of success for a pharmaceutical product requires an expectation of activity greater than a baseline level of activity. *Yamanouchi Pharmaceutical, Inc. v. Danbury Pharmacal, Inc.*, 231 F.3d 1339, 1345 (Fed. Cir. 2000).

Applicants respectfully submit that none of the references, alone or in combination, disclose, teach or suggest anything that would lead one skilled in the art to expect that a homeopathically activated form of an antibody to a PSA antigen would have any activity, let alone the specific activity levels observed. *Epshtein* does disclose that an activated form of an antibody to brain-specific antigen has some effect on rat behavior. How does this lead one skilled in the art to expect any activity of homeopathically activated antibodies to a PSA antigen, let alone the specific activity observed? None of the references, including *Epshtein* or *Davenas*, disclose a mechanism of action for the potentiated antibodies, *or contain any other information that would suggest to an artisan that what works for one type of antibodies would work for another.* While Applicants are well aware of the decision of the United States Supreme Court in *KSR Int'l v. Teleflex, Inc.* 127 S. Ct. 1727 (2007), the facts of the present case have nothing to do with a situation where "there are a finite number of identified, predictable solutions," when "a person of ordinary skill in the art has good reason to pursue the known options within his or her technical grasp." *KSR Int'l* at 1742. As it is well-known to those skilled in the art, the universe of various antigen-antibody pairs is nearly limitless.

Furthermore, to set forth a *prima facie* case of obviousness, the Examiner must show that the prior art taken in its entirety provides a reason for one skilled in the art to arrive at the invention as a whole. MPEP § 2141.02. It is improper to focus on the

specific difference between the prior art and the invention as such. *Id.* The question is whether the prior art in its entirety provides "an apparent reason to combine the known elements in the fashion claimed by the patent at issue." *KSR Int'l* at 1742. Considering the invention as a whole, the entirety of the prior art did not provide such "apparent reason." The Examiner pointed to *Feldman*'s teaching that lower doses of antibodies would "offer the advantage of lower financial costs to the patient," and asserted that this *Feldman* statement would provide a motivation to one skilled in the art to move in the direction of the claimed invention. As the specification of the present application makes explicitly clear, the claimed medicament contains "homeopathically activated form" of an antibody. The difference between the "homeopathically activated form" and the form of *Feldman* is not simply quantitative (as the Examiner appears to suggest). The difference is qualitative. At most, *Feldman* suggests a reduction in the traditional dose. How such reduction provides "an apparent reason" to cross the barrier from traditional doses to the qualitatively and intrinsically different form claimed in the amended claim 1?

Applicants submit hereby a Declaration by Dr. Oleg Epshtein ("the *Epshtein Declaration I*"). The *Epshtein Declaration I* is submitted as evidence in further response to Examiner's allegations of *prima facie* obviousness. The *Epshtein Declaration I* is submitted to show absence of *prima facie* obviousness, not in rebuttal of the alleged *prima facie* case. In the *Epshtein Declaration I*, Dr. Epshtein unequivocally states that one skilled in the art would not expect that a homeopathically activated form of an antibody to a PSA antigen would be active for intended purpose based on the information provided in the prior art at the time the '653 application was filed. Applicants respectfully assert that the *Epshtein Declaration I* is un-rebutted evidence of non-obviousness, and it provides further support for non-obviousness of amended claim 1.

Applicants respectfully suggest the Examiner did not put forth a *prima facie* case of obviousness with respect to claim 1, as amended, and dependent claims.

While Applicants believe that the evidence in the file wrapper does not support *prima facie* obviousness of amended claim 1, Applicants wish to submit rebuttal evidence to advance the prosecution on the merits. Applicants also note that a prior declaration submitted on January 9, 2008 inadvertently identified the product covered in the present

application as "Impaza," and provided information associated with Impaza. Attached herewith is another Declaration by Dr. Epshtein ("the *Epshtein Declaration II*") that supersedes the declaration filed on January 9, 2008 with respect to evidence of commercial success.

The *Epshtein Declaration II* sets forth evidence of commercial success of Afala, the product covered in the claims of the present patent application. The Court of Appeals for the Federal Circuit stated that "commercial success is relevant because the law presumes an idea would successfully have been brought to market sooner, in response to market forces, had the idea been obvious to persons skilled in the art. Thus, the law deems evidence of (1) commercial success, and (2) some causal relation or "nexus" between an invention and commercial success of a product embodying that invention, probative of whether an invention was non-obvious. *Merck & Co. v. Teva Pharms, USA*, 395 F.3d 1364, 1376 (Fed, Cir. 2005). With respect to amended claim 1, commercial success is clearly relevant. Homeopathy as an art was known for many years. Nevertheless, as showed by the evidence in the *Epshtein Declaration II*, Dr. Epshtein, who is well skilled in the art, is not aware of any successful commercial product for treatment of benign prostatic hyperplasia (BHP), apart from Afala. The evidence also shows that Afala achieved significant commercial success based on the standard in the Russian pharmaceutical market.

Applicants respectfully submit that claim 1, as amended, and dependent claims are non-obvious. Withdrawal of the rejection is respectfully requested.

In view of the foregoing, the Applicants submit that all claims are in condition for allowance. Accordingly, both reconsideration of this application and its swift passage to issuance are earnestly solicited. In the event that there are any fees due and owing in connection with this matter, please charge the same to our Deposit Account No.11-0223

Respectfully submitted,

Dated: September 29, 2008

By:/Edward D. Pergmanet/
Edward D. Pergament
(Reg. No. 43,346)
Attorney for Applicant(s)